CROSS SECTIONAL STUDY ON METABOLIC BONE DISEASE IN NONCHOLESTATIC CHRONIC LIVER DISEASE

Dissertation submitted in partial fulfillment of the requirements for the award of the degree of

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of

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY, CHENNAI, INDIA.

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CHENNAI 600003

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DECLARATION

I solemnly declare that this dissertation titled "**CROSS SECTIONAL STUDY ON METABOLIC BONE DISEASE IN NON CHOLESTATIC CHRONIC LIVER DISEASE**"is done by me in the Department of Medical Gastroenterology,Madras Medical college & Rajiv Gandhi Government General Hospital,Chennai under the guidance and supervision of professor &Head of the Department ,Department of Medical Gastroenterology,Madras Medical College & Rajiv Gandhi Government General Hospital,Chennai.This dissertation is submitted to the Tamilnadu Dr.MGR Medical University ,Chennai in partial fulfilment of the university requirements for the award of the degree of DM Medical Gastroenterology.

Place : Chennai **Dr. T.K.ANAND**

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CERTIFICATE

This is to certify that the dissertation entitled "**CROSS SECTIONAL STUDY ON METABOLIC BONE DISEASE IN NON CHOLESTATIC CHRONIC LIVER DISEASE"** is the bonafide work done by **Dr. T.K.ANAND** under our guidance and supervision in the Department of Medical Gastroenterology, Rajiv Gandhi Government General Hospital, Madras Medical College, Chennai submitted as partial fulfillment for the requirements of D.M. Degree examination Branch IV MEDICAL GASTROENTEROLOGY,AUGUST 2013,under The Dr. M.G.R. Medical University ,Chennai.

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INTRODUCTION

INTRODUCTION

Cirrhosis (chronic liver disease) represents a disorder which causes progressive hepatic fibrosis characterized by distorted liver architecture and the formation of nodules which are regenerative. Cirrhosis of any cause is usually not reversible when it is in the advanced stages at which the only option available may be liver transplantation. However, in recent times reversal of cirrhosis has been reported in several forms of liver disease following treatment of the underlying cause if detected in its early stages. Patients with cirrhosis are prone to a variety of complications.

Some of the common cause for cirrhosis are

1. Alcoholic liver disease
2. Viral hepatitis B & C
3. Autoimmune hepatitis
4. Hereditary hemochromatosis
5. Wilson's disease
6. Alfa-1 antitrypsin deficiency
7. Nonalcoholic fatty liver disease

8. Primary biliary cirrhosis
9. Primary sclerosing cholangitis

Complications of cirrhosis include [20]

1. Variceal bleed
2. Hepatic encephalopathy
3. Ascites
4. Spontaneous bacterial peritonitis
5. Hepatorenal syndrome
6. Hepatopulmonary syndrome
7. Hepatocellular carcinoma

Metabolic complications commonly encountered in patients with chronic liver disease are malnutrition, hyponatremia and metabolic bone disease.

Common chronic cholestatic liver disorders are primary sclerosing cholangitis and primary biliary cirrhosis. Hepatic osteodystrophy is known to occur in chronic

cholestatic liver diseases. Osteopenic bone disease with fracturing is a complication of chronic cholestatic liver diseases [20]. But data regarding the occurrence of metabolic bone disease (hepatic osteodystrophy) in the setting of non cholestatic chronic liver disease is scanty.

The development of metabolic bone disease in patients with primary biliary cirrhosis has, in most reports, been directly related to the duration and severity of PBC and to the intensity and duration of jaundice . However, the mechanisms which cause osteodystrophy in patients with PBC are not well understood. The plasma concentrations of vitamin D metabolites and calcium are usually normal. Biochemical and bone histomorphometric studies suggest that these patients, particularly in the precirrhotic stage, have a "low-turnover" osteoporosis, in which bone formation is inhibited and bone resorption is low or normal, although the mechanism(s) causing these changes are not known [19] .

It was initially proposed that decreased bile salt flow, leading to malabsorption of vitamin D, was responsible for the development of osteoporosis. However, this hypothesis is most likely incorrect given the observations that the plasma levels of calcidiol (25-hydroxyvitamin D) and calcitriol (1,25 dihydroxyvitamin D) are

normal in PBC patients with osteoporosis and that vitamin D replacement in the group of cases with decreased plasma concentrations will not improve the severity of osteodystrophy.

Genetic causes for osteopenia in PBC like polymorphisms in vitamin D receptor [7] , polymorphisms in IGF-1 gene and polymorphisms in collagen type Ia gene have been proposed, but now of the genetic variations were proven to be associated in most of the studies.

The diagnosis and severity assessment of osteodystrophy is done by dual energy x-ray absorptiometry (DEXA) [14] . It is a non invasive method which measures the bone mineral density. Patients are assisgned T-score and Z- score which are standard deviations below the peak and normal values. This is very useful test to screen the patients for osteodystrophy.

Data regarding the occurrence of metabolic bone disease (hepatic osteodystrophy) in the setting of non cholestatic chronic liver disease is scanty.

AIM OF THE STUDY

"To study the frequency of metabolic bone disease in noncholestatic chronic liver disease"

LITERATURE REVIEW

LITERATURE REVIEW

Osteodystrophy is a complication in patients with chronic hepatopathy, especially in those affected by chronic cholestasis. Metabolic bone disease usually manifests as osteopenia and osteoporosis. This bone disorder must be evaluated and detected early in all cirrhotic patients to minimize the risk of fractures and improve the quality of life.

EPIDEMIOLOGY

Various international studies have shown the overall incidence of metabolic bone disease in cirrhosis to be between 11% to 48%,and fracture risk due to the bone disease to be between 3%-44%.

Some of the studies which has shown the prevalence are

1. Goral *et al. 2010 – frequency of osteodystrophy was 37% in patients with cirrhosis of mixed etiology*
2. Wariaghli *et al. 2010 – frequency of osteodystrophy was 45.3% in patients with cirrhosis of mixed etiology*
3. Loria *et al. 2010 – frequency of osteoporosis was 14% and osteopenia was 26% in patients with cirrhosis of viral and alcohol etiology*

4. Sokhi *et al. 2004 – frequency of osteoporosis was 11.5% and osteopenia was 34.6% in patients cirrhosis of mixed etiology*

Chronic liver diseases which are known to cause hepatic osteodystrophy include, cholestatic liver diseases like primary biliary cirrhosis and primary sclerosing cholangitis [(20)]. Hepatic osteodystrophy can also occur in alcoholic cirrhosis and hemochromatosis.

PATHOGENESIS

The pathogenesis of hepatic osteodystrophy in patients with liver cirrhosis has not been completely understood. Several factors which includes- decreased bone formation and increased bone resorption has been recognized in liver cirrhosis. Studies have shown that increase in proinflammatory cytokines, low insulin-like growth factor, and low vitamin K lead to alterations in bone metabolism. Cytokines which are increased in cirrhosis are IL-1, IL-6 and TNF-alfa [(17)]. Serum osteocalcin levels decreases depending on reduction of osteoblast function. A decrease in serum osteocalcin levels and an increase in deoxypyridinoline (DPD) level have been observed in chronic liver disease which is the reason for the low turnover of bone mass.

Other factors responsible for reduced bone mineral deposition are

1. Vitamin K deficiency – is required for osteoblasts to synthesize osteocalcin-bone matrix protein. VitaminK deficiency leads to osteopenia in primary biliary cirrhosis and by supplementing it bone loss can be prevented [7] .
2. IGF-1 deficiency – is required for osteoblast differentiation and proliferation. IGF-1 deficiency occurring in cirrhosis and cholestatic liver disease cause osteoblast dysfunction and osteopenia [17] .
3. Hyperbilirubinemia- rise in indirect hyperbilirubinemia has shown impair osteoblast function in animal models [7] . But this is not proven in human studies.

ROLE OF CYTOKINE IN HEPATIC OSTEODYSTROPHY

Interleukin 1, Interleukin 6, TNF-alfa which is increased in chronic liver disease activates receptor activator of nuclear factor κB ligand/osteoprotegerin, which regulates bone formation by modulating osteoclast activity. Receptor activator of nuclear factor κB ligand/osteoprotegerin is upregulated in chronic liver disease

which is activated by the increased cytokines and cause increased bone resorption [17] .

Factors which increase the risk of osteodystrophy in cirrhotic patients include [7]

1. Hypogonadism
2. Vitamin D deficiency
3. Alcohol consumption
4. Chronic steroid treatment
5. Low body mass index

Contribution of vitamin D

Vitamin D has a variety of actions on minerals like calcium, phosphate, and bone metabolism. Vitamin D has an important biological effect on the enterocyte to promote differentiation and causes the intestinal absorption of calcium and phosphorus, which in turn promote bone mineralization. In high vitamin D concentrations and when there is calcium and phosphate deficiency, it also causes stimulation of bone resorption, which helps in the maintaince of supply of these ions to other tissues [6] .

Vitamin D is synthesized in the skin with exposure of ultraviolet rays from the sun; ultraviolet rays convert 7-dehydrocholesterol to vitamin D. Anyone with reduced exposure to the sun is prone to vitamin D deficiency. Calcidiol, is formed in the liver before being converted in the kidneys into metabolic active vitamin D (calcitriol).

Gastrointestinal causes of vitamin D deficiency include gastrointestinal malabsorption, associated with disorders of the small intestine, pancreatic diseases resulting in decreased absorption of vitamin D and hepatobiliary disease causes depletion of endogenous 25OHD stores due to abnormal enterohepatic circulation. Malabsorption of vitamin D results as a consequence of steatorrhea, which reduces fat emulsification and chylomicron-facilitated absorption [(6)] . Vitamin D deficiency may be associated with rickets or osteomalacia. Patients affected are asymptomatic or may exhibit a reduction in bone volume rather than causing defective bone mineralization.

In liver failure, the levels of 25-OH vitamin D can be reduced due to impaired synthesis. However, liver function needs to be severely compromised for it to cause reduced 25-OH vitamin D synthesis [(7)] .

Subclinical vitamin D insufficiency is common in the setting of chronic liver disease and could contribute to the formation of osteoporosis or osteopenia by decreasing absorption of calcium [6].

Vitamin D deficiency is usually associated with secondary hyperparathyroidism, and there is increased bone turnover and accelerated loss of bone mass. Factors which contribute to vitamin D deficiency include Intestinal malabsorption, altered enterohepatic circulation of vitamin D and reduced skin synthesis in patients with jaundice.

CLINICAL FEATURES

Patients with metabolic bone disease are usually symptomatic and they are picked up during routine screening.

When symptoms do occur, they are related to fractures. The most common fractures are vertebral fractures, two-thirds of which are asymptomatic and are diagnosed as incidental findings on a chest or abdominal x-ray. In some patients, vertebral fractures may result in loss of height, kyphosis, or acute back pain. Other fractures seen in patients with osteoporosis include hip fractures and distal radius fractures

FRACTURE RISK ASSESSMENT

Facture risk has to determined in patients with metabolic bone disease irrespective of the cause. Patients with osteoporosis and osteopenia are at increased risk for facture [3]. Risk factors independent of bone mineral density include

1. Previous history of fracture
2. Increased age
3. Long-term glucocorticoid therapy
4. Low body weight < 58 kg
5. Family history of hip fracture
6. Smoking
7. Excess alcohol intake

DIAGNOSIS OF METABOLIC BONE DISEASE

Bone mineral density determines the bone strength. Determinants of bone strength, which are not dependent on bone mineral density are bone turn over, microarchitecture of bone like trabacular thickness, cortical thickness and cortical porosity, matrix properties and mineralizaton.

Investigation for bone strength will give an insight on the pathogenesis of osteoporosis and osteopenia and gives a better understanding on the treatment given for osteoporosis. Investigations like micro CT and MRI are being developed which can discern individual trabeculae are being developed. With these investigations fracture risk can be accurately gauged. As of now the gold standard for the diagnosis of metabolic bone disease is by DEXA scan [6].

Bone mineral density testing — BMD testing is the most commonly used clinical test to diagnose osteoporosis, osteopenia, predict the risk for fracture, and monitor response to therapy. BMD testing can be done on various sites of the body and predict fracture risk. Dual-energy x-ray absorptiometry (DEXA SCAN) of the spine, hip, and forearm is the method for diagnosis of osteoporosis [14]. Serial monitoring of bone mineral density over a period is essential because

1. There has been a strong correlation between bone mineral density measured by DEXA scan and mechanical strength.
2. Studies have shown relationship between bone mineral density by DEXA scan and fracture risk.
3. Randomized clinical trails have shown drug therapy based on the bone mineral density measurement has reduced fracture risk.

4. Accuracy and precision of bone mineral density measured by DEXA scan is very good.

5. Radiation exposure with DEXA scan is very low.

WHO CRITERIA FOR METABOLIC BONE DISEASE

severe osteoporosis – BMD > 2.5 SD below the reference with one or more fractures

osteoporosis – BMD > 2.5 SD below the reference

osteopenia – BMD between 1 and 2.5 SD below the reference

normal – BMD < 1 SD of the reference

Dual-energy x-ray absorptiometry technology — A typical DEXA scan machine consists of a padded table on which the patient should lie and a movable C-arm with an x-ray tube under the patient and a detector above the patient. The x-ray tube, which is below the patient generates photon beams of two different energy levels, for which is called "dual-energy" source. A collimator below the table controls the scatter of the photons and directs the photons towards the area of interest. The difference in attenuation that is the reduction in intensity of the two photon beams as they go through body tissue of variable composition and distinguishing bone from soft tissue and allows quantification of bone mineral density. Denser and thicker tissue contains more electrons and will not allow many photons to pass through to the detector. A computer which is specially designed with its proprietary software designed by each manufacturer forms a complete DEXA scan.

Radiation exposure to the patient is very minimal, usually of a similar magnitude to daily background radiation. Radiation which is scattered beyond the edge of the DEXA table is negligible. Shielding of the technologist or the room is not necessary. But as a safety precaution, the technologist doing the DEXA scan

should typically not sit within three feet of the table edge when the patient is being scanned.

DEXA measures bone mineral content (in gms) and bone area (in square centimeters), then calculates "areal" BMD in g/cm2 by dividing bone mineral content and bone area. T-score, the value used for diagnosis of osteoporosis, is calculated by subtracting the mean BMD of a young-adult reference population from the patient's BMD and dividing by the standard deviation (SD) of young-adult population. Z-score, used to compare the patient's BMD to a population of peers, is calculated by subtracting the mean BMD of an age-, ethnicity-, and sex-matched reference population from the patient's BMD and dividing by the SD of the reference population. The mean BMD and SD of the reference populations used for these calculations is a critical variable in the determination of T-scores

There are significant differences in the technologies used by different manufacturers and sometimes different models of DEXA made by the same manufacturer. Manufacturers use different methods for creating dual photon beams (eg, K-edge filtering and voltage switching), different bone edge detection algorithms, different assumptions on body size and tissue composition, different calibration, and different types of photon detectors. Photon beams have different configurations, eg, pencil beam and fan beam. The bone regions of interest (ROI) measured may be different, especially so with the femoral neck. The reference

databases used to calculate T-scores and Z-scores may be different. For all of these reasons, it is not possible to make quantitative comparisons of BMD measured on different instruments, especially those made by different manufacturers, unless a cross-calibration study has been done

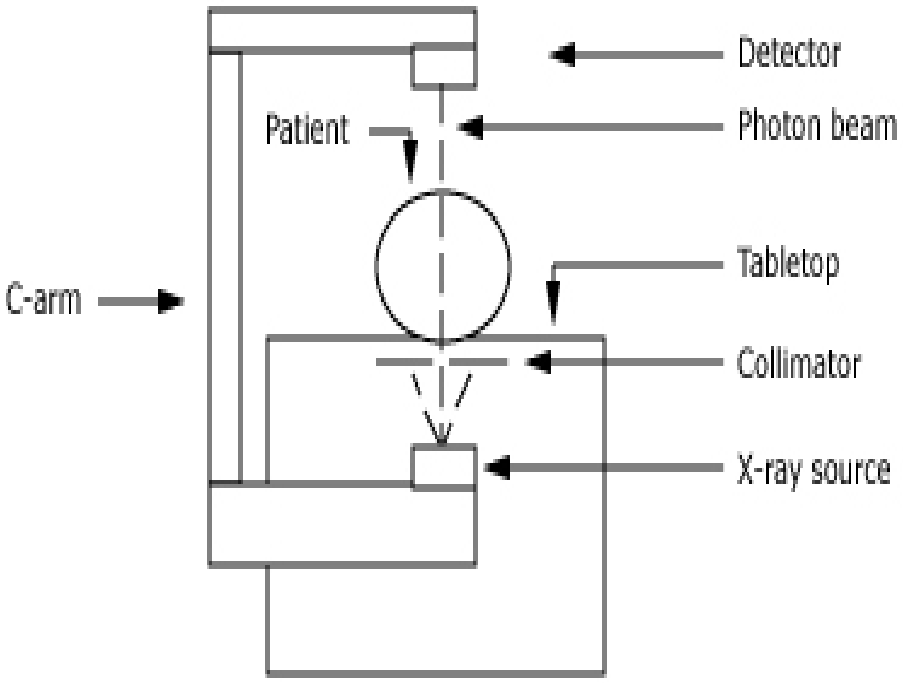


Figure 1 – dual energy x-ray absorptimetry.

Other methods to analyze bone mineral density

1. **Quantitative CT –** cortical and trabecular bone can be assessed by determining the volume of bone density. It can measure the bone density of hip and spine. This test can be used to assess the treatment reponse and is also being used is research setup. This method is ot used for routine screening. Drawbacks of this test are, it cannot assess the risk of fracture and is a very expensive test.

2. **Ultrasound** - Patients at risk for osteoporosis can be identified with use of quantitative ultrasound, which is a reasonable predictor of fracture risk. This method can be used in mass screening setup and there is no risk of radiation. But ultrasound threshold cutoff for DEXA score has not been having good sensitivity and specificity. This test cannot be used as confirmatory test and always one has do DEXA scan in suspected patients to confirm low bone mineral density. Since with ultrasound only the peripheral sites can be measured it cannot be used as a tool for follow up of patients who are on therapy. In current clinical practice quantitative ultrasound can only be used in mass screening and clinical research.

SITE OF MEASUREMENT OF BONE MINERAL DENSITY

Most common site for measurement of bone mineral density are HIP and SPINE. Spine measurement is more accurate and fracture risk can be assessed more precisely. In patients with cirrhosis and ascites, measurement of bone mineral density of spine can be falsely positive, due to the fluid in the abdomen. In these patients with ascites measurement of bone mineral density from the hip will be useful to assess the risk of fracture [8].

Other sites of bone mineral density measurement include the peripheral site like calcaneum and wrist. Methods by which the measurement can be done are portable DEXA scan, x-ray absorptiometry and ultrasound.

These methods by which the peripheral bone mineral density is measured are not validated and the only method validated by the WHO is DEXA scanning of the hip or spine. Only place where the peripheral measurement is used is, in the setting of mass screening.

SCREENING FOR BONE MINERAL DENSITY LOSS

Screening for osteoporosis has to be done in all patients with chronic cholestatic disease. DEXA scan should be advised once a year and follow up of patients on treatment for osteoporosis or osteopenia can be done with DEXA scan every 2 years [16].

There are few studies showing the incidence of osteoporosis in chronic liver disease with varying etiology to be between 11 to 48%. So, screening for osteodystrophy in cirrhotic patients can reduce the fragile fractures and can lead to improvement in the quality of life.

Post liver transplant patients are prone for bone disease and increased risk of fractures, so it is advisable to screen all patients awaiting liver transplant, in order to give them the appropriate treatment and reduce fracture risk.

TREATMENT

General treatment includes non pharmacologic measures like diet rich in vitamin D, light exercises and smoking cessation.

Smoking is major risk factor for osteodystrophy and smoking cessation considerably decreases the risk of fractures.

Calcium and vitamin D supplementation should be done to maintain bone density.

Calcium in the dose of 1000 mg /day and the dose of vitamin D is 800 U/day [21].

Pharmacological therapy for metabolic bone disease

Bisphosphonates — Alendronate (10 mg/day or 70 mg once weekly [orally]) or risedronate (5 mg/day, 35 mg once weekly, or 150 mg once monthly), and ibandronate (150 mg once monthly [orally] or 3 mg intravenously every three months) [22].

Zoledronic acid (ZA), 5 mg administered intravenously (IV) once yearly, is also effective for osteodystrophy.

Severe esophagitis can occur with this group of drugs and it can be prevented by taking large amounts of water and being upright for 1 hour.

Bisphosponates are the main treatment in patients with severe metabolic bone disease , even though there is very limited data on its use in cirrhosis.

Selective estrogen receptor modulators — Raloxifene [22] is a tissue selective estrogen receptor modulator (SERM) that is used for the prevention and treatment

of osteoporosis. It increases bone mineral density and reduces the risk of vertebral fractures. Raloxifene also appears to lower the risk of breast cancer, does not stimulate endometrial hyperplasia or vaginal bleeding, and increases the risk of venous thromboembolism. Although it decreases serum total and low-density-lipoprotein (LDL) cholesterol concentrations, raloxifene does not appear to affect the risk of coronary heart disease.

Raloxifen is one of the first-line drugs for prevention of osteoporosis. However, it is somewhat less effective than estrogen and bisphosphonates, although direct fracture prevention comparisons are lacking. There are nonskeletal considerations with raloxifene that may play an important role in the selection of patients for preventive therapy. Raloxifene reduces breast cancer risk but increases thromboembolic events and hot flashes.

Parathyroid hormone — Parathyroid hormone (PTH) seems an unlikely candidate for the treatment of osteoporosis because of its well-described deleterious effect on bone. However, intermittent administration of recombinant human PTH (both full-length 1-84 or fragment 1-34) stimulates bone formation more than resorption and is effective for fracture reduction in women with

osteoporosis. This topic is reviewed in detail elsewhere.PTH is also effective in men with osteoporosis.

Some of the newer medications which are used to treat bone mineral loss include

1. Denosumab-which is a monoclonal antibody directed against the receptor responsible for bone resorption. Osteoclasts are inhibited by this medication.
2. Strontium ranelate – it is drug which is being tried in animal models and it acts by decreasing bone resorption. Based upon changes in markers of bone formation and resorption in postmenopausal women with osteoporosis, it appears to have a modest antiresorptive effect, with little effect on bone formation

MATERIAL AND METHODS

Study design – cross sectional study

Subjects :

32 patients with the diagnosis of non cholestatic liver disease attending our department were included and 10 healthy subjects were taken as controls were taken in this study.

All the patients and controls were explained in detail about the study, and an informed consent was obtained.

EXCLUSION CRITERIA

1. Patients with cholestatic liver disease
2. Patients who were on calcium supplements and vitamin D
3. Patients on medications which affect bone mineral density
4. Postmenopausal women
5. Patients with coexistent chronic kidney disease

Patients enrolled in the study were evaluated for the cause for liver disease.

Evaluation included

1. Hepatitis B
2. Hepatitis C
3. Wilson's disease
4. Alcoholic liver disease
5. Autoimmune hepatitis
6. Iron studies

Biochemical analysis

Blood for biochemical analysis was drawn from all patients enrolled in the study. After an overnight fast for 10 hours, blood for analysis was drawn in the morning. Biochemical analysis included liver function test, prothrombin time, renal function test, serum calcium, serum phosphosus, parathyroid hormone and vitamin D.

Liver function test, renal function test and prothrombin time analysis were done by automated method. Calcium estimation was done by arsenazo III method,and phosphorus was estimated by ammonium molybdate method. Parathyroid hormone and vitamin D were estimated by chemiluminescence immumunoassay (CIA).

BONE MINERAL DENSITY MEASUREMENT

All patients and controls included in the study were subjected to bone mineral density measurement by dual energy x-ray absorptiometry (DEXA). Dual energy x-ray absorptiometry was done by using HOLOGIC-QDR4500 machine.

Patients and controls were classified as having normal BMD or osteopenia or osteoporosis using the WHO criteria.

SEVERITY OF LIVER DISEASE

Severity assessent of the liver disease in patients with cirrhosis was done by Child Pugh score and Model for End Stage Liver Disease (MELD) scores [20].

Figure 2 – HOLOGIC-QDR 4500 dual energy x-ray absorptiometry.

Observation and Results

Sex distribution

In the study, there were 32 patients with cirrhosis and 10 normal controls. Out of the 32 patients, there was 22 male patients (68.8%) and 10 female patients (31.3%). In the control group, there were 6 males (60%) and 4 females (40%).

Table 1

Sex	Group				Total	
	Cases		Controls			
	N	%	N	%	N	%
Male	22	68.8	6	60.0	28	66.7
Female	10	31.3	4	40.0	14	33.3
Total	32	100.0	10	100.0	42	100.0

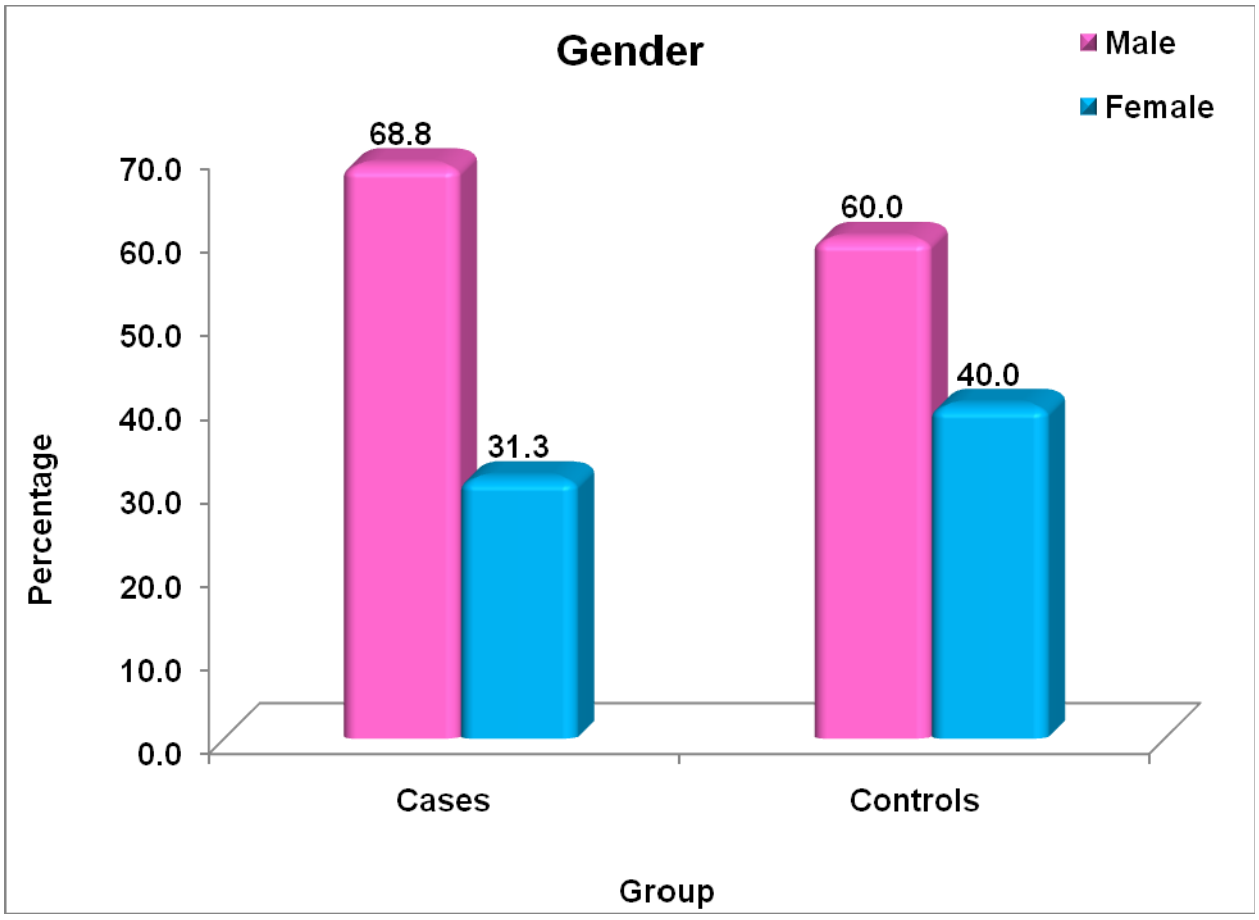

Gender
Male
Female
68.8
31.3
60.0
40.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
Percentage
Cases
Controls
Group

Chart 1

Age group

Average age of the patients was 38.97 yrs.

Average age ot the controls was 42.50 yrs.

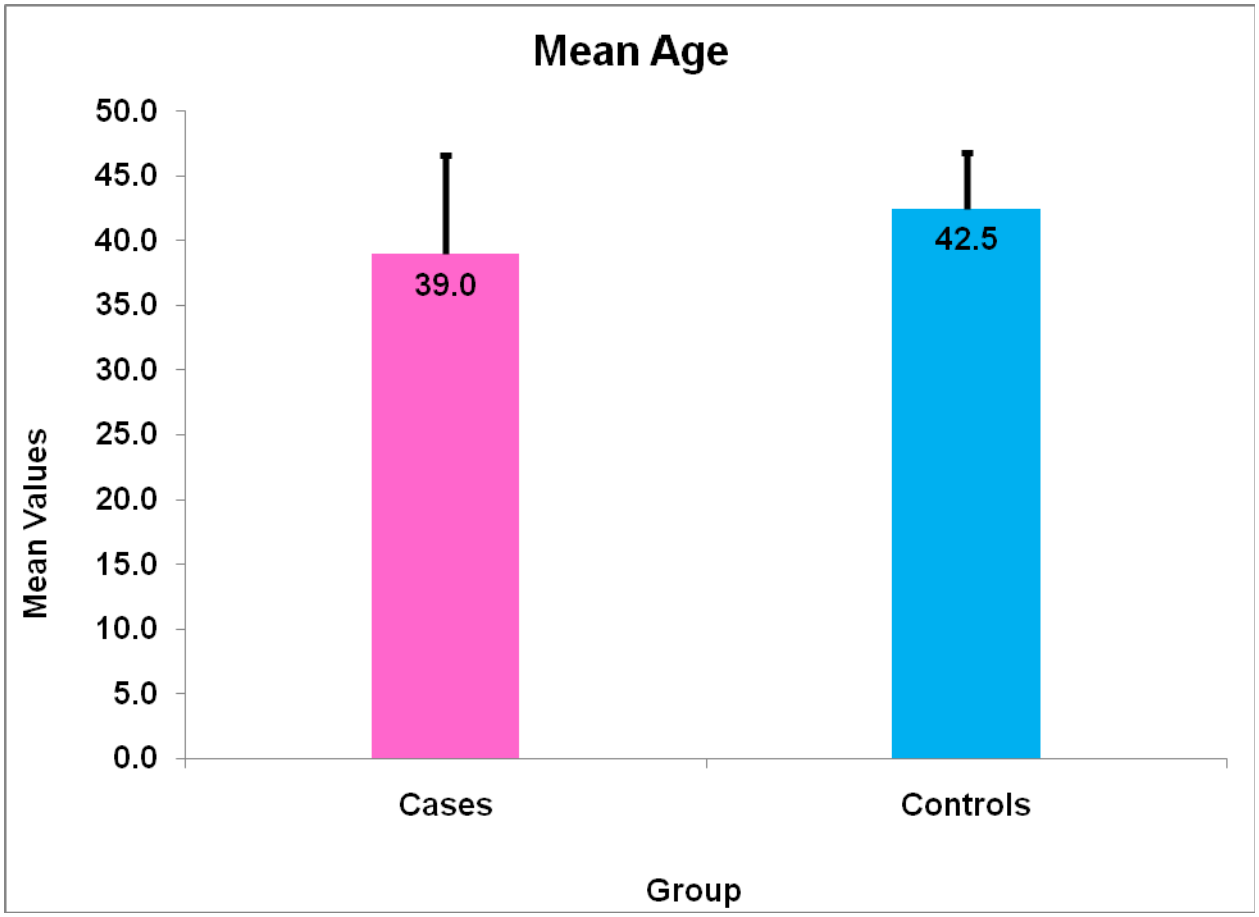


Chart 2

Comparison of biochemical variables between cases and controls

Mean bilirubin level in the cirrhosis group was 1.31 and in the control group it was 0.88.

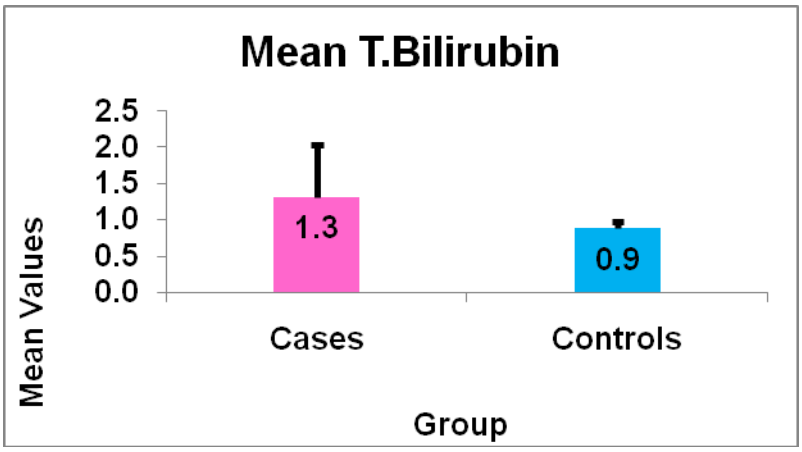


Chart 3

Mean alkaline phosphatase level in the cirrhosis group was 131.3 and in the control group it was 80.1.

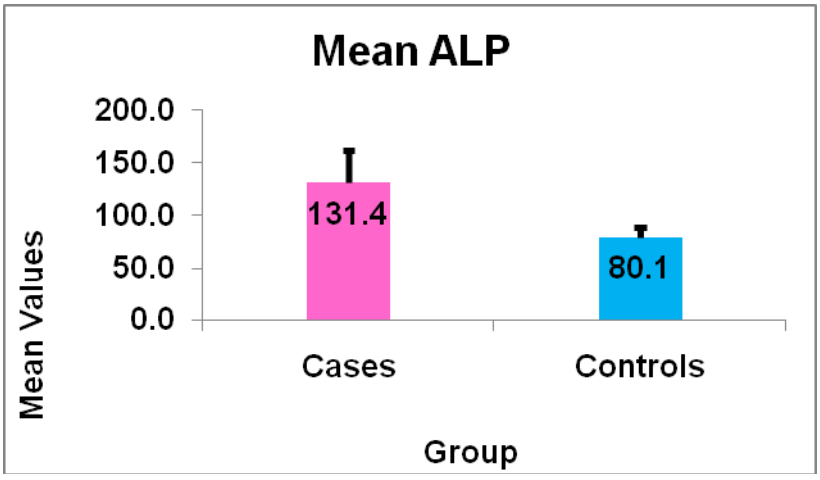


Chart 4

Mean values of SGOT and SGPT were 62.81 and 58.75 respectively in the cirrhosis group and in the control group it was 21.90 and 20.20 respectively.

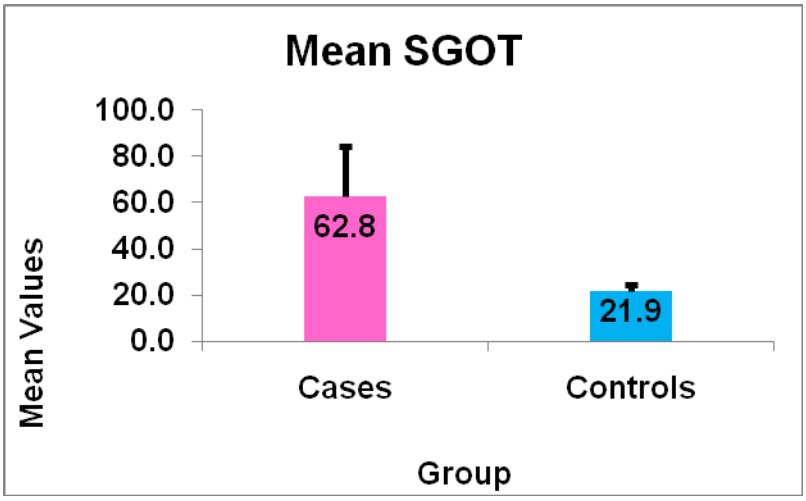


Chart 5

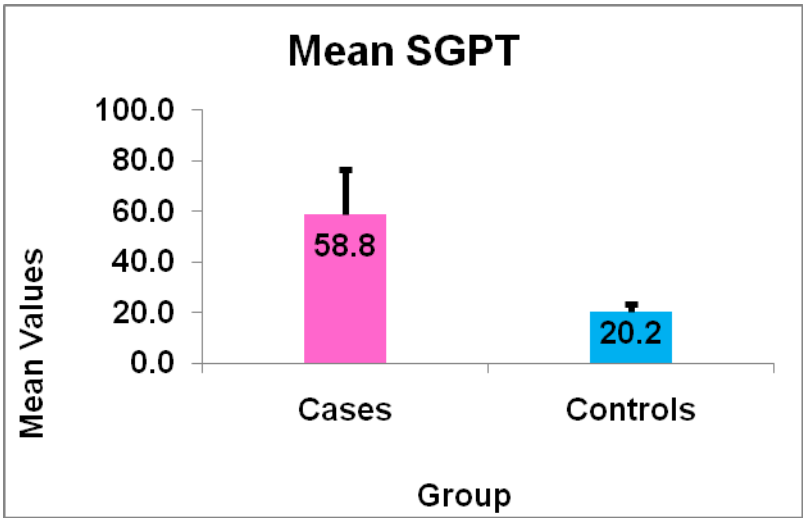


Chart 6

Mean value of albumin in the cirrhosis group was 3.38 and in the control group it was 3.97.

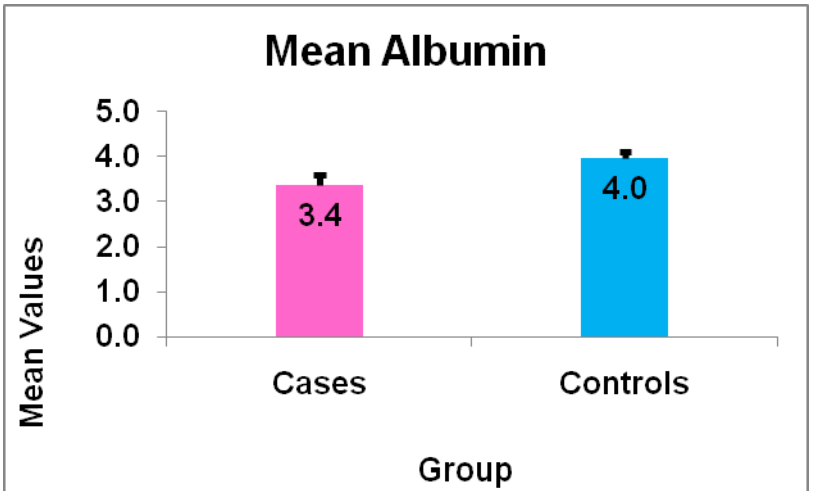


Chart 7

Mean value of INR (prothrombin time) in the cirrhosis group was 1.4 and in the control group it was 0.9.

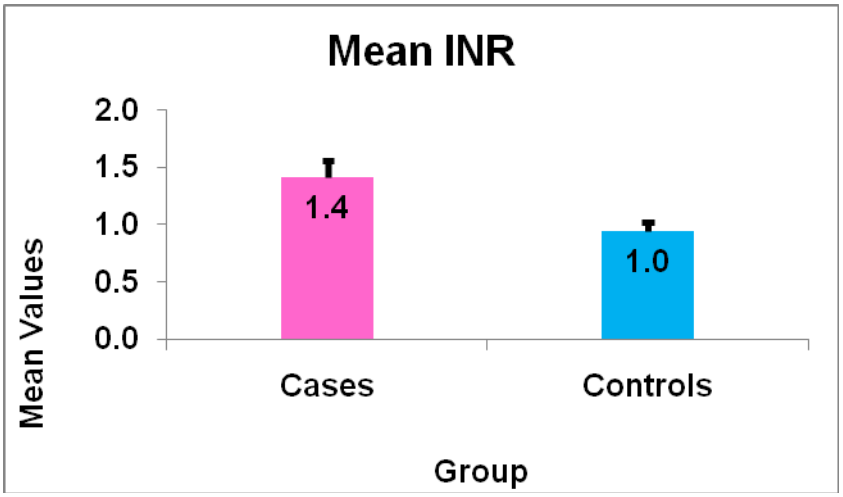


Chart 8

Calcium and phosphorus levels were decreased in the chronic liver disease group than the control group. Mean value of calcium and phosphorus in the cirrhotic group was 7.9 and 3.4 respectively and in the control group it was 9.7 and 3.7.

Calcium was corrected according the albumin levels and was computed.

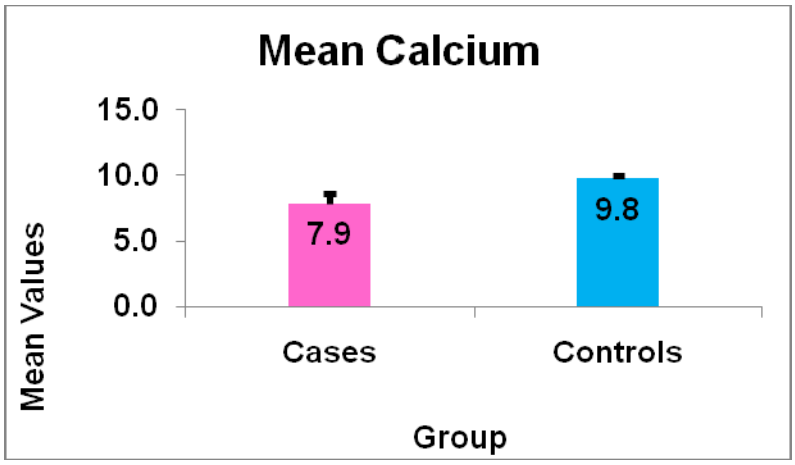


Chart 9

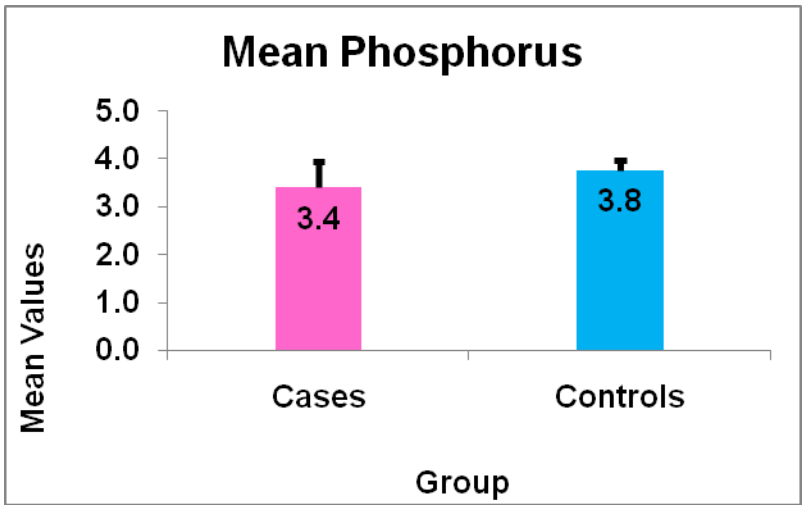


Chart 10

Parathyroid hormone was with in the normal range in both the cirrhotic group and controls, but the mean value was higher in the cirrhotic group than the control group.

Mean value of parathyroid hormone was 40.17 in the cirrhotic group and 33.6 in the control group with a P value of 0.026, which was significant.

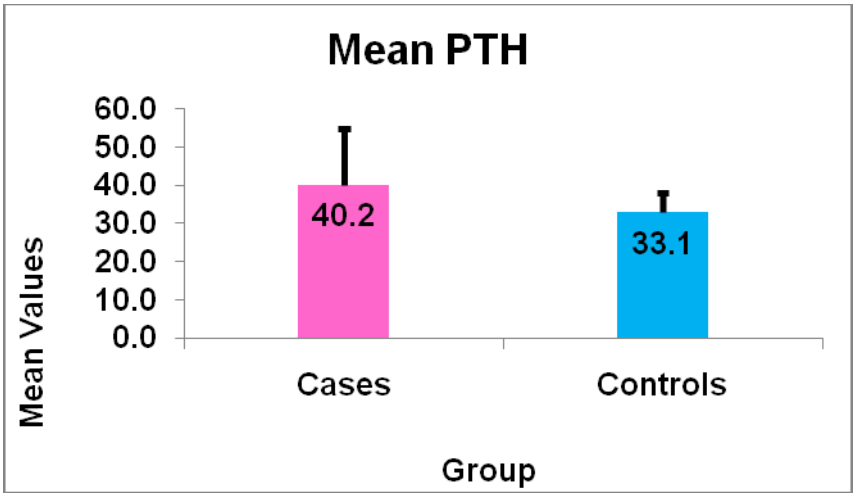


Chart 11

Vitamin D levels was significantly lower in the cirrhotic group than the control group. Mean value of vitamin D in the cirrhotic group was 23.9 and in the control group it was 41.5 with a P value of 0.001, which was significant.

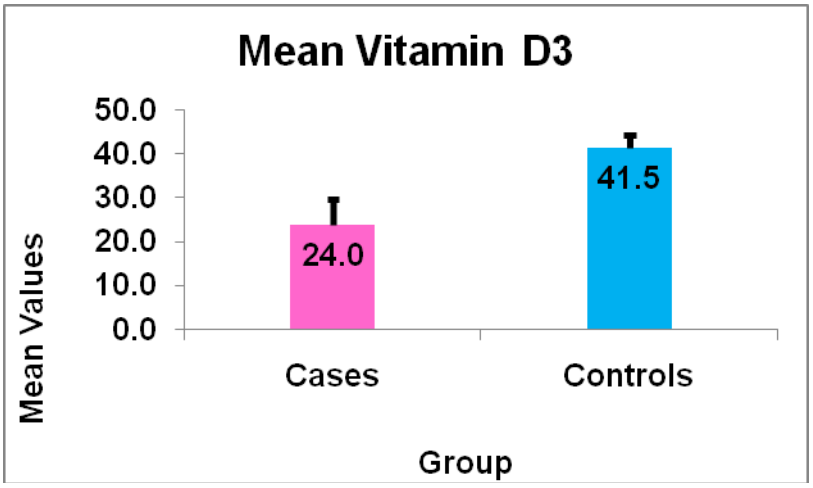


Chart 12

Table 2 -demographic and biochemical parameters between cirrhotic group and control group

		N	mean	Standard deviation (SD)
Age	Cases	32	38.97	7.618
	Controls	10	42.50	4.301
T.Bilirubin	Cases	32	1.312	0.730
	Controls	10	0.880	0.092
ALP	Cases	32	131.38	30.880
	Controls	10	80.10	9.291
SGOT	Cases	32	62.81	21.650
	Controls	10	21.90	2.601
SGPT	Cases	32	58.75	17.678
	Controls	10	20.20	3.490
Albumin	Cases	32	3.381	0.209
	Controls	10	3.970	0.149
INR	Cases	32	1.416	0.148
	Controls	10	0.950	0.071

Calcium	Cases	32	7.903	0.726
	Controls	10	9.770	0.221
Phosphorus	Cases	32	3.406	0.539
	Controls	10	3.770	0.206
PTH	Cases	32	40.175	14.826
	Controls	10	33.050	5.061
Vitamin D3	Cases	32	23.988	5.880
	Controls	10	41.530	2.767

Primary end point

Low bone mineral density in the form of osteoporosis and osteopenia was noted in 24 out of 32 patients . 8 patients out of the 32 patients in the cirrhotic group had no osteodystrophy. Among the control group none of the patients had low bone mineral density.

Among the 24 patients with deceased bone mineral density in the cirrhotic group 2 patients had osteoporosis (6.3%) and 22 patients had osteopenia (68.8%) classified according to the WHO classification.

There was a significant number of patients who had low bone mineral density in the cirrhotic group compared to the controls, with a P value of 0.001, which is statistically significant.

Table 3

Dexa scan	Group				Total	
	Cases		Controls			
	N	%	N	%	N	%
Normal	8	25.0	10	100.0	18	42.9
Osteopenia	22	68.8	0	.0	22	52.4
Osteoporosis	2	6.3	0	.0	2	4.8
Total	32	100.0	10	100.0	42	100.0

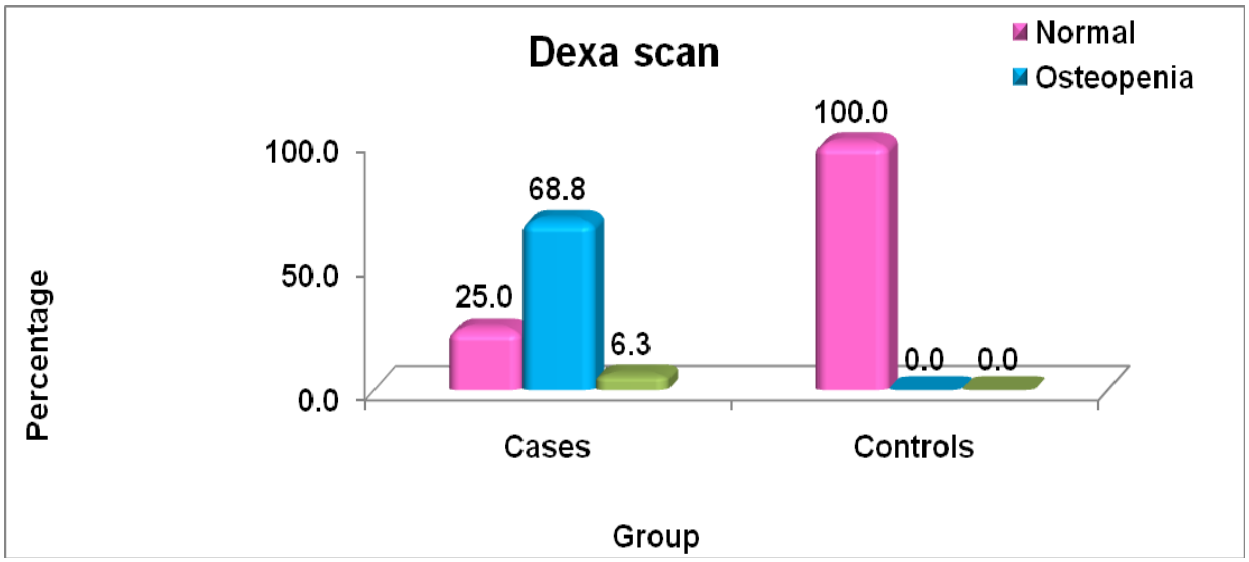


Chart 13

Picture - 1

ACEER Associates in Clinical Endocrinology Education and Research

Name: Bhuvaneswari, Rajasekaran	Sex: Female	Height: 159.8 cm
Patient ID: R-7594	Ethnicity: Asian	Weight: 78.4 kg
DOB: 23 April 1968	Menopause Age: 37	Age: 43

Referring Physician: Dr.Usha Sriram

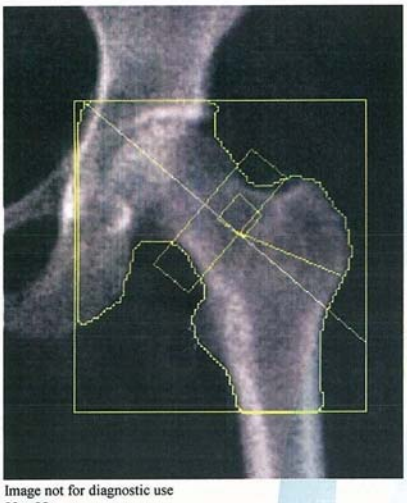


Image not for diagnostic use
93 x 99

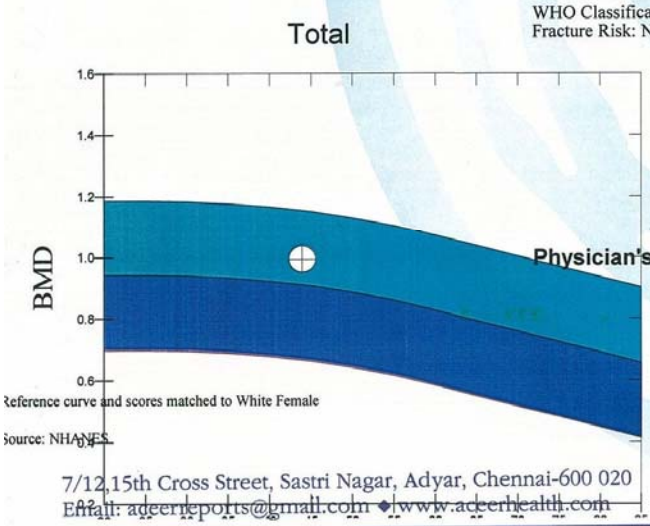
Scan Information:

Scan Date: 04 April 2012 ID: A04041207
Scan Type: f Left Hip
Analysis: 04 April 2012 15:02 Version 12.3
Left Hip
Operator: U.K.
Model: QDR 4500A (S/N 45013)
Comment:

DXA Results Summary:

Region	Area (cm²)	BMC (g)	BMD (g/cm²)	T - Score	Z - Score
Neck	5.00	4.55	0.910	0.5	0.9
Troch	7.23	5.27	0.730	0.3	0.5
Inter	18.03	20.25	1.123	0.1	0.3
Total	**30.26**	**30.07**	**0.994**	**0.4**	**0.7**
Ward's	1.12	0.84	0.748	0.1	0.9

Total BMD CV 1.0%
WHO Classification: Normal
Fracture Risk: Not Increased



Reference curve and scores matched to White Female

Source: NHANES

Physician's Comment:

7/12,15th Cross Street, Sastri Nagar, Adyar, Chennai-600 020
Email: aceerreports@gmail.com ◆ www.aceerhealth.com
Ph: 044 24460762/63 ◆ Fax: 044 24460760/61

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Picture - 2

ACEER Associates in Clinical Endocrinology Education and Research

Name: VENKATESH T	Sex: Male	Height: 171.6 cm
Patient ID: DR.ANAND	Ethnicity: Asian	Weight: 61.7 kg
DOB: 12 December 1982		Age: 30

Referring Physician: DR.ANAND

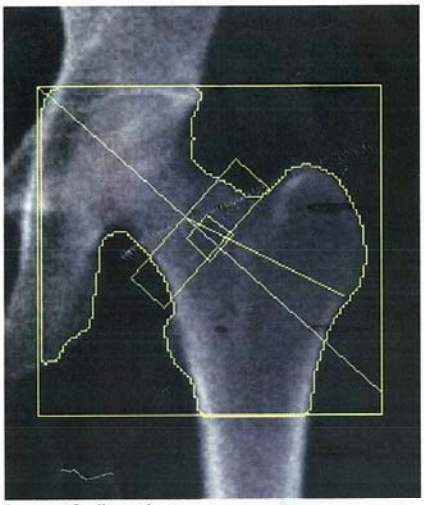

Image not for diagnostic use
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Scan Information:

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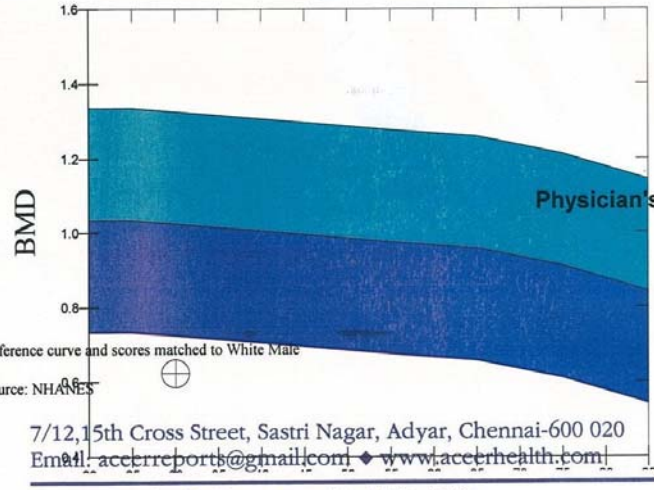
Scan Type: f Left Hip
Analysis: 13 December 2012 13:34 Version 12.3
Left Hip
Operator: U.K.
Model: QDR 4500A (S/N 45013)
Comment:

DXA Results Summary:

Region	Area (cm^2)	BMC (g)	BMD (g/cm^2)	T - Score	Z - Score
Neck	5.07	3.06	0.603	-2.4	-2.2
Troch	12.02	5.49	0.456	-2.5	-2.5
Inter	19.22	14.07	0.732	-2.6	-2.5
Total	**36.31**	**22.61**	**0.623**	**-2.7**	**-2.7**
Ward's	1.17	0.49	0.417	-2.6	-2.4

Total BMD CV 1.0%
WHO Classification: Osteoporosis
Fracture Risk: High

Total



Reference curve and scores matched to White Male
Source: NHANES

Physician's Comment:

7/12,15th Cross Street, Sastri Nagar, Adyar, Chennai-600 020
Email: acelrreports@gmail.com ◆ www.acelrhealth.com
Ph: 044 24460762/63 ◆ Fax: 044 24460760/61

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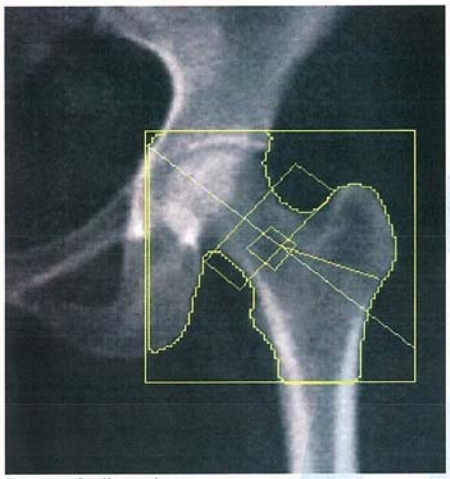
Picture - 3

ACEER Associates in Clinical Endocrinology Education and Research

Name: BANUMATHY S	Sex: Female	Height: 145.0 cm
Patient ID: DR.ANAND	Ethnicity: Asian	Weight: 39.2 kg
DOB: 20 July 1986		Age: 26

Referring Physician: DR.ANAND



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78 x 81

Scan Information:

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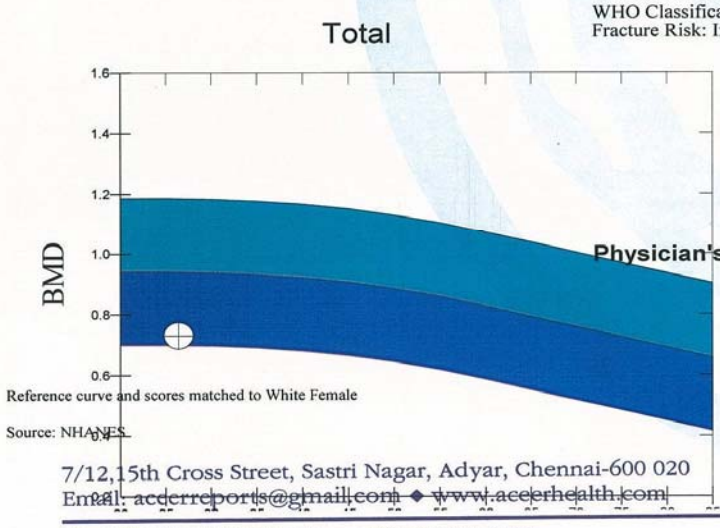
Scan Type: f Left Hip
Analysis: 18 December 2012 12:45 Version 12.3
Left Hip
Operator: U.K.
Model: QDR 4500A (S/N 45013)
Comment:

DXA Results Summary:

Region	Area (cm²)	BMC (g)	BMD (g/cm²)	T - Score	Z - Score
Neck	3.76	2.14	0.569	-2.5	-2.5
Troch	6.78	3.79	0.559	-1.4	-1.4
Inter	11.36	10.07	0.887	-1.4	-1.3
Total	**21.90**	**16.00**	**0.731**	**-1.7**	**-1.7**
Ward's	1.12	0.53	0.474	-2.2	-2.2

Total BMD CV 1.0%
WHO Classification: Osteopenia
Fracture Risk: Increased



Reference curve and scores matched to White Female

Source: NHANES

Physician's Comment:

7/12,15th Cross Street, Sastri Nagar, Adyar, Chennai-600 020
Email: acderreports@gmail.com ◆ www.aceerhealth.com
Ph: 044 24460762/63 ◆ Fax: 044 24460760/61

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Among the patients with low bone mineral density in the cirrhotic group, 15 were male patients and 9 were female patients.

Of the 8 patients with normal bone mineral density in the cirrhotic group, there was 7 male patients and 1female patient.

Table 4

Sex	Dexa scan				Total	
	Normal		Osteopenia			
	N	%	N	%	N	%
Male	7	87.5	15	62.5	22	68.8
Female	1	12.5	9	37.5	10	31.3
Total	8	100.0	24	100.0	32	100.0

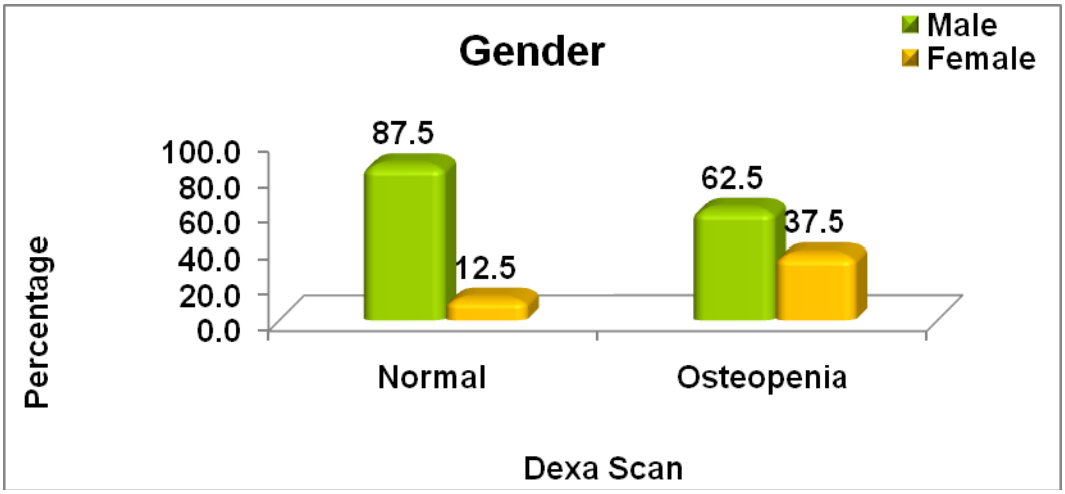

Chart 14

Etiology of cirrhosis in the study group, who had low bone mineral density was alcoholic liver disease in 5 patients (20.8%), hepatitis B related cirrhosis in 8 patients (33.3%) and cryptogenic in 11 patients (45.8%).

In patients with normal bone mineral density the etiology was alcoholic liver disease in 5 patients (62.5%), hepatitis B related cirrhosis in 1 patient (12.5%) and cryptogenic in 2 patients (25%).

Table 5

Aetiology	Dexa scan				Total	
	Normal		Osteopenia			
	N	%	N	%	N	%
Alcohol	5	62.5	5	20.8	10	31.3
HBV related	1	12.5	8	33.3	9	28.1
Cryptogenic	2	25.0	11	45.8	13	40.6
Total	8	100.0	24	100.0	32	100.0

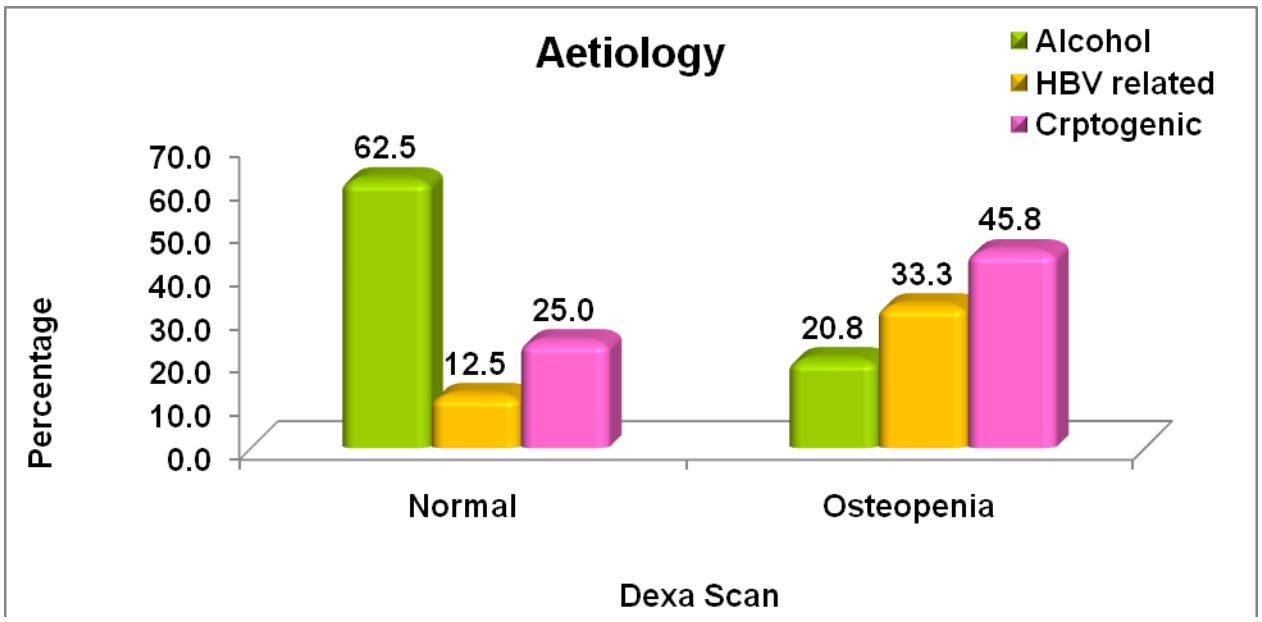

Chart 15

All patients in the cirrhotic group with normal bone mineral density had CTP stage A.

Of the 22 patients with low bone mineral density in the cirrhosis group, 14 patients had a CTP class A (58.3%), 8 patients had CTP class B (33.3%) and 2 patients had CTP class C (8.3%). P value for correlation of severity of cirrhosis was 0.119, which was not statistically significant , but could be clinically significant in view of the small sample size.

Table 6

CTP score	Dexa scan				Total	
	Normal		Osteopenia			
	N	%	N	%	N	%
A	8	100.0	14	58.3	22	68.8
B	0	.0	8	33.3	8	25.0
C	0	.0	2	8.3	2	6.3
Total	8	100.0	24	100.0	32	100.0

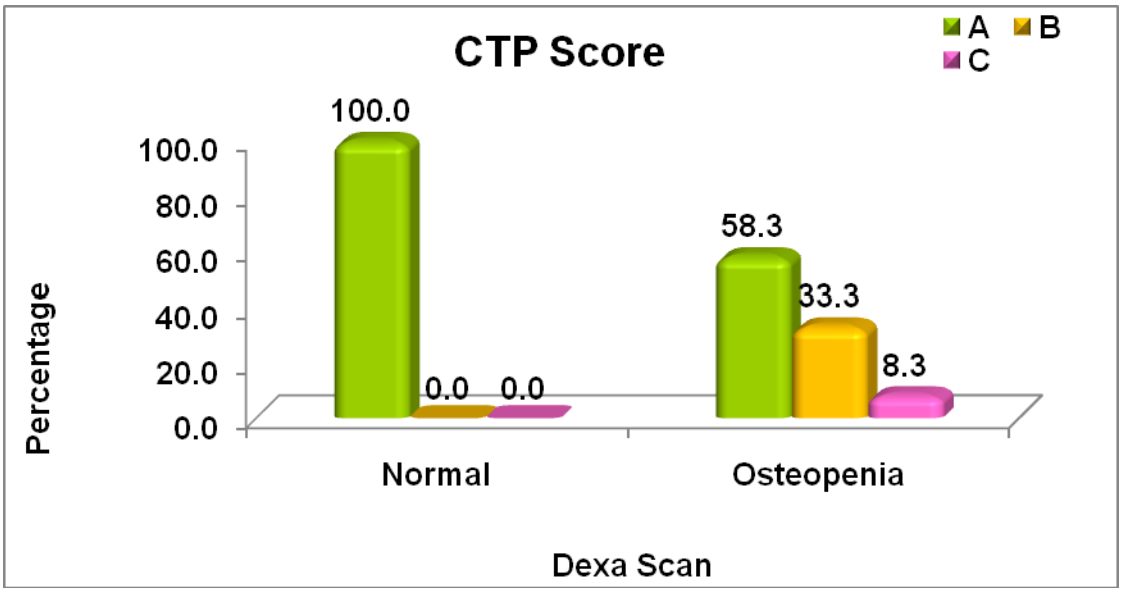

Chart 16

Comparison of variables in patients with normal BMD and low BMD

Average age of patients with normal bone mineral density was 39.1 years. Average age of patients with low bone mineral density was 38.9 years.

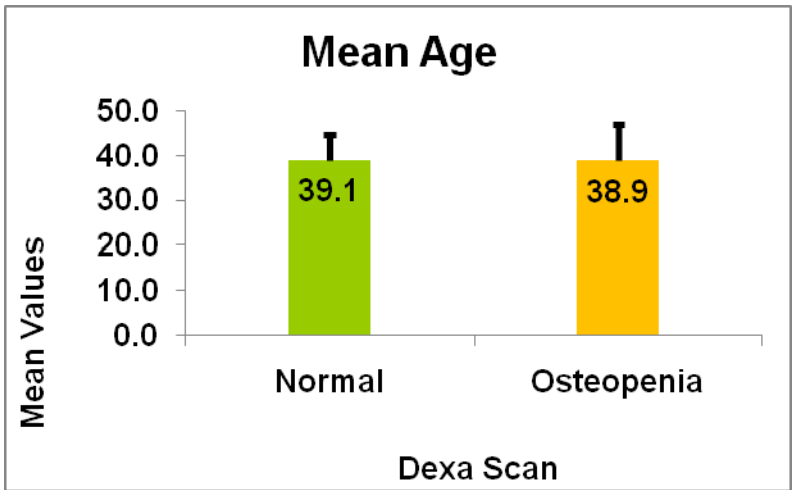

Chart 17

Patients with low bone mineral density in the cirrhotic group were symptomatic for a significant longer period of time compared to the patients with normal bone mineral density. Mean duration of symptoms in low bone mineral density group was 2.1 months and in normal bone mineral density group it was 14.8 months, with a P value of 0.001, which was significant.

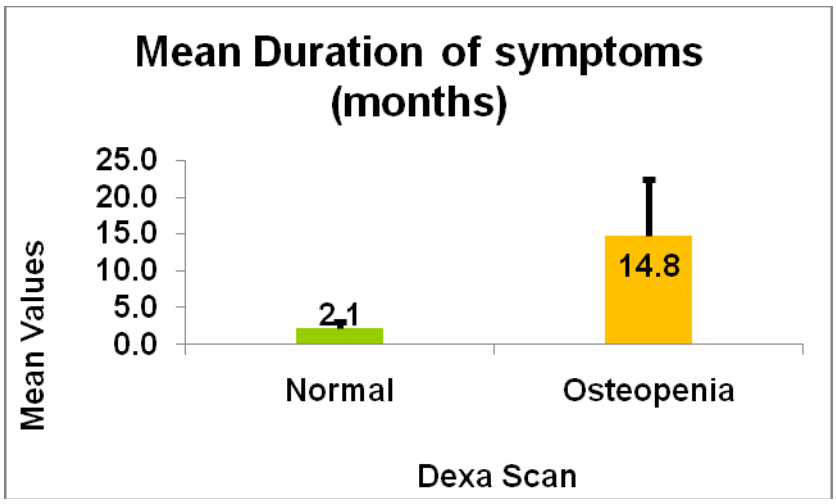

Chart 18

Bilirubin levels was lower in patients with normal bone mineral density than in patients with low bone mineral density. Mean bilirubin value in the low bone mineral density group was 1.42 and in the normal bone mineral density group it was 0.96, with a P value of 0.017, which was significant.

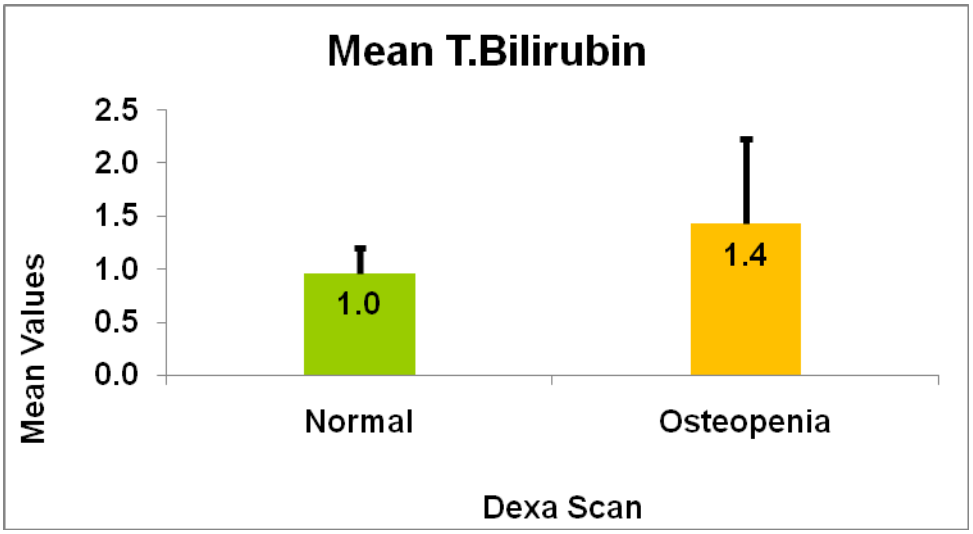

Chart 19

Mean values of alkaline phosphatase, SGOT, SGPT and albumin were not significantly different in patients with low and normal bone mineral density.

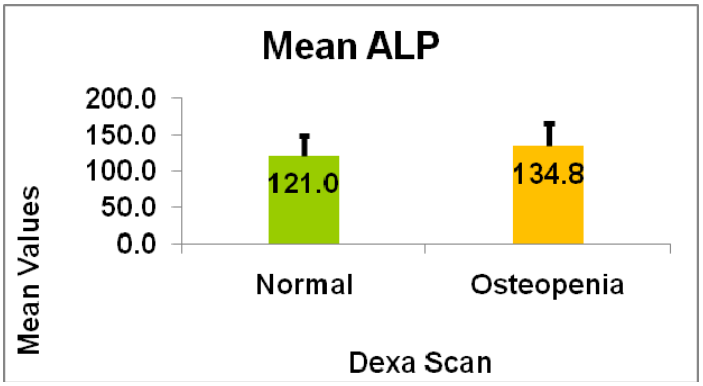

Chart 20

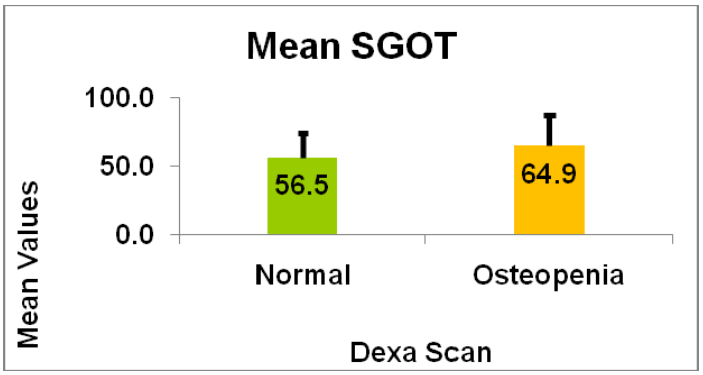

Chart 21

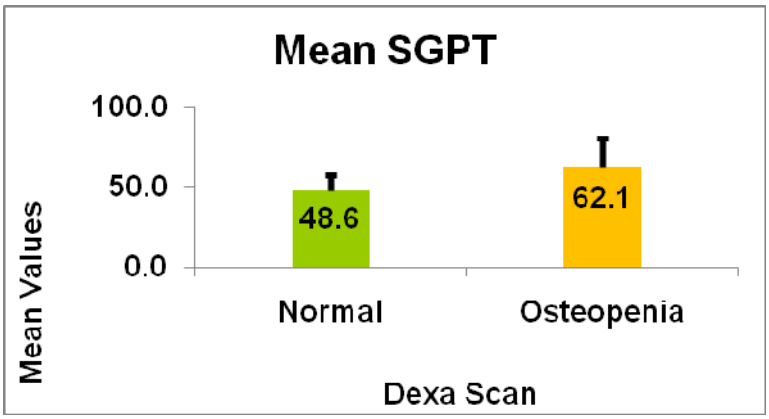

Chart 22

Mean INR in the normal bone mineral density group was 1.31 and in the low bone mineral density group it was 1.45, with a P value of 0.021, which was significant.

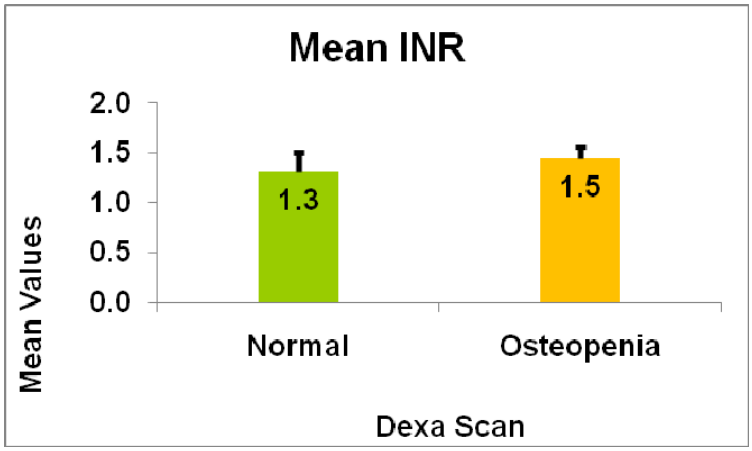

Chart 23

Mean values of calcium, phosphorus, parathyroid and Vitamin D in patients with normal bone mineral density group was 7.9, 3.5, 37.5 and 25.0 respectively and in the low bone mineral density group it was 7.8, 3.3, 41, 23.6 respectively.

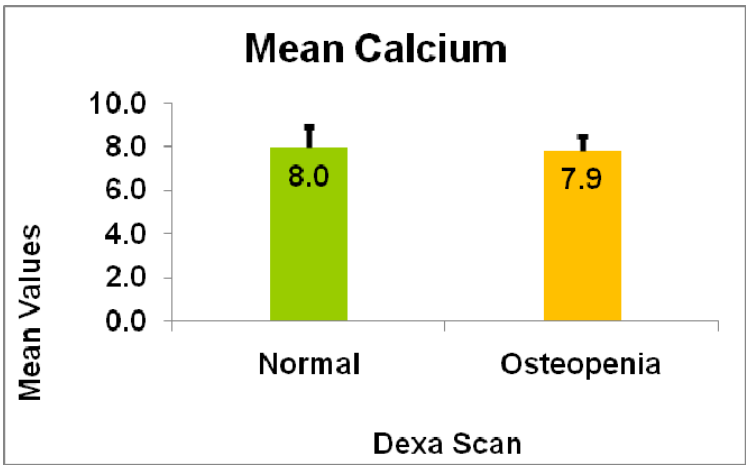

Chart 24

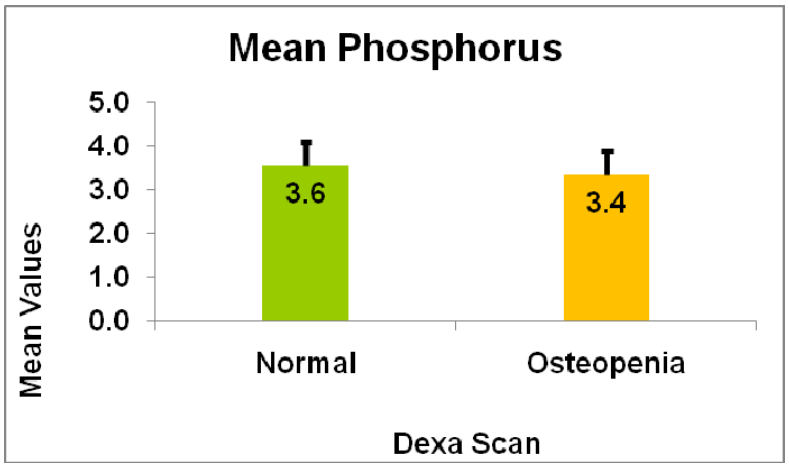

Chart 25

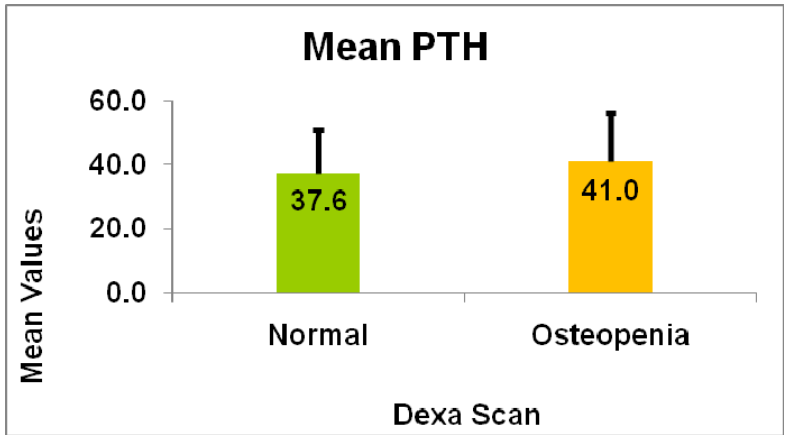

Chart 26

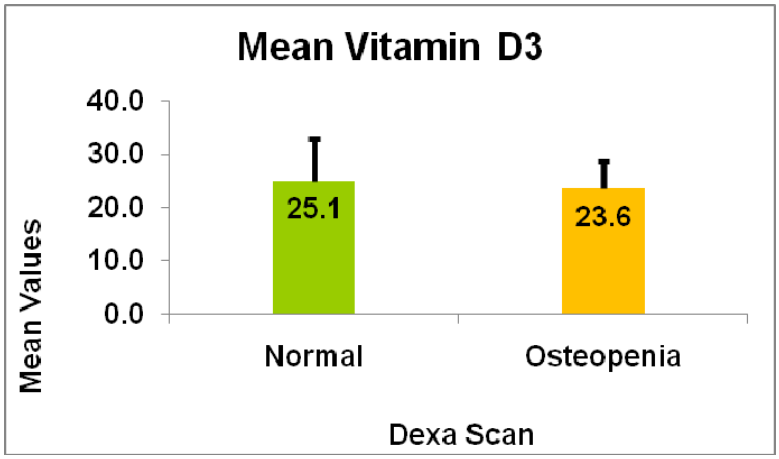

Chart 27

Table 7- Comparison of Demographic and Biochemical Parameters between patients with low BMD and normal BMD.

	Dexa scan	N	Mean	Std. Deviation	P-Value
Age	Normal	8	39.130	5.718	0.948
	Osteopenia	24	38.920	8.262	
Duration of symptoms (s)	Normal	8	2.130	0.991	0.001
	Osteopenia	24	14.830	7.510	
T.Bilirubin	Normal	8	0.963	0.239	0.017
	Osteopenia	24	1.429	0.802	
ALP	Normal	8	121.000	27.718	0.280
	Osteopenia	24	134.830	31.647	
SGOT	Normal	8	56.500	18.095	0.349
	Osteopenia	24	64.920	22.664	
SGPT	Normal	8	48.630	8.991	0.060
	Osteopenia	24	62.130	18.683	
Albumin	Normal	8	3.450	0.131	0.289
	Osteopenia	24	3.358	0.226	
INR	Normal	8	1.313	0.189	0.021
	Osteopenia	24	1.450	0.118	

Calcium	Normal	8	7.988	0.958	0.711
	Osteopenia	24	7.875	0.654	
Phosphorus	Normal	8	3.575	0.534	0.315
	Osteopenia	24	3.350	0.541	
PTH	Normal	8	37.563	13.558	0.573
	Osteopenia	24	41.046	15.400	
Vitamin D3	Normal	8	25.089	7.895	0.550
	Osteopenia	24	23.621	5.203	
MELD	Normal	8	10.250	1.165	0.103
	Osteopenia	24	11.790	2.484	

DISCUSSION

DISCUSSION

Metabolic bone disease (hepatic osteodystrophy) is one the metabolic complication associated with cirrhosis. With improvement in management of chronic liver disease patients and with more number of liver transplantation being done these days, it is imperative to maintain a good quality of life in these patients [1],[10]. One of the factors which cause a decrease in quality of life, in patients with cirrhosis is decrease in bone mineral density, by increasing the risk of fragile fractures. But most of the patients with metabolic bone disease are not recognized, as there is no proper screening done in these patients.

In our study, there was a significant number of cirrhotic patients who had decreased bone mineral density. In a study from India, Joe Goerge et al [5] has reported 68% prevalence of low bone mineral density in chronic liver disease patients. Another study from Chandigarh, Choudhary et [15] al has shown the prevalence of low bone mineral density in non cholestatic chronic liver disease to be around 80%. In our study, we had 68.8% of the cirrhotic patient to have osteopenia and 6.3% of the patients to have osteoporosis.

Lumbar spine and femur neck are the common sites to measure bone mineral density, as it is composed of more trabecular bone. But in patients with cirrhosis, due the presence of ascites measuring bone mineral density in the lumbar spine is controvertial. Guanabans.N et al [8] has shown that measuring bone mineral density in the lumbar spine is highly inaccurate giving false positive reports. In our study we had taken the femur neck as site of measurement to avoid false positive reports.

Etiology of hepatic osteodystrophy can be multifactorial [4]. In our study, we found that the mean values of bilirubin and prothrombin time [3] was significantly higher in patients with low bone mineral density compared with those patients with normal bone mineral density (P values of 0.017 and 0.02 respectively). Vitamin D levels were significantly low in the cirrhotic patients than the controls (P value - 0.001), but there was no significant difference in the levels between the patients with low bone mineral density and normal bone mineral density (P value – 0.55). Correlation of vitamin D levels with low bone mineral density has not been established in previous studies. In our study also there was no significant correlation of vitamin D levels between the low and normal bone mineral density patients.

Similarly no significant correlation was observed with calcium, phosphorus and parathyroid hormone between the low bone mineral density and normal bone mineral density patients. Tukeli et al [9] has also shown that there is no correlation with bone mineral density and calcium, albumin and GGT.

In our study, the common etiology of cirrhosis among patients who had low bone mineral density was hepatitis B (8 patients) [13], followed by alcohol (5 patients). No cause was found in 11 patients with low bone mineral density. Study by Choudhary et al [15] has shown the etiology of cirrhosis to be viral in 41.1% and alcohol in 58.2%.

In our study the duration of symptoms in the cirrhotic group significantly correlated with the presence and severity of bone mineral density. Severity of cirrhosis had a significant correlation to the bone mineral loss. All patients with CTP class B and C had low bone mineral density. 2 patients in the study with CTP class C had osteoporosis and 8 patients with CTP class B had osteopenia (P value – 0.119), eventhough the P value was not statistically significant it could be clinically significant due to small sample size of our study. But a study by Ashraful et al [12] has shown no relation between the severity of liver disease and bone mineral loss. So we would require more studies on this issue.

CONCLUSION

CONCLUSION

Inference from this study done in our department include

1. Hepatic osteodystrophy was common in people with non cholestatic chronic liver disease.
2. There was a slight male predominance noted in the study.
3. Bilirubin and prothrombin levels were significantly low in patients with low bone mineral density compared to patients with normal bone mineral density.
4. Longer duration of symptoms in the cirrhotic patients was significantly related to the bone mineral loss.
5. Severity of the liver disease was significantly related to the bone mineral loss.
6. There was no correlation of vitamin D, calcium, parathyroid hormone levels with bone mineral loss.
7. In view of high frequency of metabolic bone disease in patients with non cholestatic chronic liver disease, screening for bone mineral loss with DEXA scan should be done.

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BIBLIOGRAPHY

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Key words

1. PBC	-	Primary biliary cirrhosis
2. IGF	-	Insulin Like Growth Factor
3. DEXA	-	Dual Energy Xray Absorpiometry
4. IL	-	Interleukin
5. TNF	-	Tumor Necrosis Factor
6. CT	-	Computerized Tomography
7. MRI	-	Magnetic Resonance Imaging
8. BMD	-	Bone Mineral Density
9. LDL	-	Low Density Lipoprotein
10. PTH	-	Parathyroid Hormone
11. CTP	-	Child Turcotte Pugh
12. SGOT	-	Serum Glutamic oxaloacetic Transaminase
13. SGPT	-	Serum Glutamic Pyruvate Transaminase
14. INR	-	International Normalized Ratio

PROFORMA

NAME OF THE PATIENT :

AGE:

IP NO.:

ADDRESS:

OCCUPATION:

HISTORY:

EXAMINATION:

INVESTIGATIONS : CBC

RFT

LFT

URINE R/E

USG ABDOMEN

PORTAL DOPPLER

VIRAL MARKERS

CALCIUM/PO4 :

VIT. D:

PTH:

BMD:

CTP SCORE:

MELD SCORE:

COMPLICATIONS:

DIAGNOSIS:

சுய ஒப்புதல் படிவம்

ஆய்வு செய்யப்படும் தலைப்பு

ஈரல் கரணை நோயினால் ஏற்படும் எலும்பு மாற்றங்களை அறிந்து கொள்ள நடத்தும் ஆய்வு

ஆராய்ச்சி நிலையம் : வயிறு மற்றும் குடல் சார்ந்த மருத்துவப் பிரிவு,
இராஜீவ் காந்தி அரசு பொது மருத்துவமனை மற்றும்
சென்னை மருத்துவக் கல்லூரி,
சென்னை - 600 003.

பங்கு பெறுபவரின் பெயர் : உறவுமுறை :

பங்கு பெறுபவரின் எண். :

பங்கு பெறுபவர் இதனை (✓) குறிக்கவும்

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களைப் பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் இவ்வாய்வில் தன்னிச்சையாகத்தான் பங்கேற்கிறேன். எந்தக் காரணத்தினாலோ எந்தக் கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகிக் கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்மந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும்போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளைப் பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும் அதைப் பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்குக் கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன், இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ அல்லாத எதிர்பாராத வழக்கத்திற்கு நோய்க்குறி தென்பட்டாலோ உடனே அதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்கிறேன். ☐

இந்த ஆய்வில் எனக்கு இரத்தத்தில் பரிசோதனை செய்து கொள்ள நான் முழு மனதுடன் சம்மதிக்கிறேன். ☐

பங்கேற்பவரின் கையொப்பம்..... இடம்..... தேதி
கட்டைவிரல் ரேகை

பங்கேற்பவரின் பெயர் மற்றும் விலாசம்.....

ஆய்வாளரின் கையொப்பம்..... இடம்..... தேதி

ஆய்வாளரின் பெயர்.....

Bµõ´a] uPÁÀ uõÒ

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Bµõ´a]¯õÍº øPö¯õ¨£® £[÷PØ£õÍº øPö¯õ¨£®

÷uv :

CONSENT

DESCRIPTION: You are invited to participate in a research study on liver disease.

PROCEDURES: : You will be asked to provide a sample of blood (6 ml). The blood will be drawn from your arm . your bone mineral density will be measured by DEXA scan at the same time.

PAYMENTS: You will not be paid to participate in this study.

I, _____ , hereby consent to donate a sample of my blood for the purpose of estimating calcium, phosphorus, vitamin D and parathormone and undergo a scan to measure my bone density . I have understood that this sample and the scan report will be used for research and the results will not be available to me. I have also understood that this does not involve any additional procedure

Signature of the patient

Name of the patient

Witness – Signature, Name and address

INFORMATION SHEET

We are conducting a cross sectional study “to determine the frequency of metabolic bone disease in Non-cholestatic chronic liver diseases” at Department of Gastroenterology, Madras Medical College . Government General Hospital, Chennai.

We will be measuring bone mineral density for all the patients with Non-cholestatic chronic liver diseases . Blood for Biochemical analysis will be drawn.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in loss of benefits to which you are otherwise entitle.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of the Investigator Signature of the Participant

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No : 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. T.K. Anand
PG in DM Medical Gastroenterology
Madras Medical College, Chennai -3

Dear Dr. T.K. Anand

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "To study the prevalence of metabolic bone disease in chronic liver disease patients " No.20092012.

The following members of Ethics Committee were present in the meeting held on 13.09.2012 conducted at Madras Medical College, Chennai -3.

1. Dr. S.K. Rajan. M.D.,FRCP.,DSc	-- Chairperson
2. Prof. Pregna B. Dolia MD Vice Principal, Madras Medical College, Chennai -3 Director , Institute of Biochemistry, MMC, Ch-3	-- Member Secretary
3. Prof. B. Vasanthi MD Professor of Pharmacology ,MMC, Ch-3	-- Member
4. Prof. M. Reghu MD Director, Inst. Of Internal Medicine, MMC, Ch-3	-- Member
5. Prof. MD. Ali. MD.DM Prof & HOD of MGE, MMC, Ch-3	-- Member
6. Prof. P. Karkuzhali. MD Director i/c, Prof., Inst. of Pathology, MMC, Ch-3	-- Member
7. Prof. Bavani Shankar. MS Prof of General Surgery, MMC, Ch-3	-- Member
8. Thiru. S. Govindsamy. BABL	-- Lawyer
9. Tmt. Arnold Soulina MA MSW	-- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

CROSS SECTIONAL STUDY ON METABOLIC BONE DISEASE IN NON CHOLESTATIC CHRONIC LIVER DISEASE

Dissertation submitted in partial fulfillment of the requirements for the award of the degree of

DM(MEDICAL GASTROENTEROLOGY)

BRANCH - IV

of

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY, CHENNAI, INDIA.

MADRAS MEDICAL COLLEGE,

CHENNAI 600003

August 2013

INTRODUCTION

Cirrhosis (chronic liver disease) represents a disorder which causes progressive hepatic fibrosis characterized by distorted liver architecture and the formation of

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CROSS SECTIONAL STUDY ON METABOLIC BONE DISEASE IN NON CHOLESTATIC CHRONIC LIVER DISEASE Dissertation submitted in partial fulfillment of the requirements for the award of the degree of DM(MEDICAL GASTROENTEROLOGY) BRANCH - IV of THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY, CHENNAI, INDIA. MADRAS MEDICAL COLLEGE, CHENNAI 600003 August 2013 INTRODUCTION Cirrhosis (chronic liver disease) represents a disorder which causes progressive hepatic fibrosis characterized by distorted liver architecture and the formation of nodules which are regenerative. Cirrhosis of any cause is usually not reversible when it is in the advanced stages at which the only option available may be liver transplantation....

name of the patient	age	sex	diagnosis	aetiology	duration of	T.Bilirubin	ALP	SGOT	SGPT	albumin	INR	calcium	phosphorus	PTH	vitamin D3	dexa scan	CTP score	MELD
suresh	37	m	cirrhosis	alcohol	2 mts	0.8	134	42	38	3.6	1.5	9.8	2.7	31.3	40	normal	A	11
vijayakumar	40	m	cirrhosis	alcohol	8 mts	1	98	68	57	3.4	1.4	8.4	3.9	38.6	20.9	osteopenia	A	10
sajitha	45	f	cirrhosis	crptogenic	10 mts	0.9	142	59	63	3.1	1.5	7.4	4.4	52.5	25.4	osteopenia	A	11
devaraj	48	m	cirrhosis	alcohol	1 mt	1.3	98	75	48	3.3	1.3	8.1	4.1	23.4	22.39	normal	A	10
vellamuthu	49	m	cirrhosis	alcohol	24 mts	2.3	163	81	72	3.5	1.6	7.4	2.7	47.2	30.33	osteopenia	B	15
selvam	40	m	cirrhosis	crptogenic	7 mts	1.6	198	40	38	3.6	1.4	6.9	4.4	21.5	22.47	osteopenia	A	12
irudhayanathan	45	m	cirrhosis	hbv related	8 mts	3.9	105	54	46	2.9	1.8	9.6	2.8	4.6	8.71	osteopenia	C	19
rajalaksmi	23	f	cirrhosis	crptogenic	9 mts	0.9	113	74	84	3.7	1.3	7.2	3.7	55.4	20.07	osteopenia	A	11
sudhakar	30	m	cirrhosis	crptogenic	4 mts	0.8	98	32	43	3.5	1.1	7.2	3.9	32.3	15.92	normal	A	9
kumar	45	m	cirrhosis	alcohol	10 mts	0.7	179	78	53	3.4	1.4	7.9	3.3	35.8	21.4	osteopenia	A	10
appar	47	m	cirrhosis	hbv related	24 mts	1.2	99	45	62	3.5	1.4	7.9	3.4	39.1	27.42	osteopenia	A	11
sriranjani	40	f	cirrhosis	crptogenic	24 mts	1	102	32	41	3.1	1.4	8.5	4	33.6	20.2	osteoporosis	B	11
vannamal	38	f	cirrhosis	crptogenic	2 mts	0.8	94	38	47	3.6	1.5	8.1	3.9	68.7	19.2	normal	A	11
annamalai	39	m	cirrhosis	hbv related	10 mts	3.2	116	102	93	3.4	1.6	7.9	3.6	33	20.8	osteopenia	B	17
narayanaswamy	45	m	cirrhosis	alcohol	1 mt	1.1	147	82	63	3.3	1.5	8.8	4.1	38.5	22.5	normal	A	12
dhanalaksmi	41	f	cirrhosis	hbv related	16 mts	1.2	134	58	64	3.4	1.4	8.6	3.4	28.2	35.6	osteopenia	A	11
meganathan	42	m	cirrhosis	alcohol	2 mts	0.9	172	67	52	3.5	1.3	7.8	3.1	40.2	33.8	normal	A	9
govindaraj	40	m	cirrhosis	alcohol	36 mts	2.1	181	73	53	3.3	1.5	7.9	2.7	81.1	22.7	osteopenia	C	14
thangaraj	47	m	cirrhosis	crptogenic	10 mts	1	109	59	68	3.1	1.6	7.8	3.2	37.1	20.5	osteopenia	A	12
bakthan	38	m	cirrhosis	hbv related	2 mts	1.3	112	62	59	3.5	1.3	6.9	3.1	33.8	23.5	normal	A	11
indrani	31	f	cirrhosis	crptogenic	7 mts	0.8	96	47	61	3.6	1.4	7.8	2.9	52.3	25.5	osteopenia	A	10
mehaboob basha	42	m	cirrhosis	alcohol	14 mts	0.9	165	67	62	3.5	1.3	6.6	3.5	40	18.9	osteopenia	B	9
rajaiyyan	35	m	cirrhosis	alcohol	3 mts	0.7	113	54	39	3.3	1	7.2	3.7	32.3	23.4	normal	A	9
thanunathan	43	m	cirrhosis	hbv related	15 mts	1.1	121	92	87	3.1	1.4	6.8	2.9	29.9	20.5	osteopenia	B	11
arasani rangan	35	f	cirrhosis	hbv related	13 mts	1.1	132	45	49	3.6	1.5	8.7	2.4	66.8	28.6	osteopenia	A	11
venkakesh	30	m	cirrhosis	crptogenic	24 mts	0.8	99	94	71	3.2	1.3	7.9	3.9	45.9	23.4	osteoporosis	B	9
chandrasekar	50	m	cirrhosis	crptogenic	15 mts	0.9	124	37	41	3.4	1.3	8.1	3.3	28.7	27	osteopenia	B	9
stella	33	f	cirrhosis	crptogenic	10 mts	0.8	156	38	32	3.5	1.4	7.8	2.9	33.7	25.6	osteopenia	A	10
banumathy	26	f	cirrhosis	crptogenic	10 mts	1.4	118	96	90	3.3	1.5	7.8	3.1	42	20.8	osteopenia	A	11
venkatesan	23	m	cirrhosis	crptogenic	24 mts	1.8	153	112	97	3.6	1.4	8.3	3.2	54.8	29.8	osteopenia	A	12
vijayalaksmi	30	f	cirrhosis	hbv related	18 mts	2.1	188	65	71	2.9	1.5	7.7	3.9	34.9	22.8	osteopenia	B	14
srinivasan	50	m	cirrhosis	hbv related	10 mts	1.6	145	42	36	3.5	1.5	8.1	2.9	48.4	27.5	osteopenia	A	13

name of the patient	age	sex	T.Bilirubin	ALP	SGOT	SGPT	albumin	INR	calcium	phosphorus	PTH	Vitamin D	dexa scan
senthil kumar	32	m	0.8	76	24	27	3.9	0.9	9.8	4.1	24.6	42.3	normal
jayanthi	40	f	0.9	87	22	19	4	1	10.1	3.9	28.7	40.1	normal
ramani	42	m	0.7	98	23	18	4.2	0.9	9.7	4	31.8	39.7	normal
shankar	47	m	1	65	18	23	4.1	1.1	9.8	3.7	29.8	38.9	normal
sivaiah	45	m	0.9	72	27	21	3.8	0.9	10	3.9	33.7	42.5	normal
natarajan	43	m	0.8	83	20	19	4.1	1	9.9	3.7	41.8	39.6	normal
bhuvaneswari	45	f	0.9	74	19	16	3.8	0.9	9.6	3.8	38.3	45.7	normal
kanchana	41	f	1	86	22	18	3.8	0.9	9.7	3.5	37.6	43.6	normal
sastri	44	m	0.9	77	21	24	4.1	1	9.8	3.6	32.8	37.6	normal
manoram	46	f	0.9	83	23	17	3.9	0.9	9.3	3.5	31.4	45.3	normal